

## **I. AMENDMENT**

### **IN THE SPECIFICATION:**

*Please delete the paragraph extending from line 14 to line 27 of page 1 and replace it with the following paragraph:*

Gene expression profiling processes are commonly used to represent a cell's physiological response to a particular compound, treatment, or disease. For example, a January 1, 1999 article by Iyer et al., Volume 283, Science, at pages 83-87 (~~www.sciencemag.org~~), discloses the use of a temporal program of gene expression to represent a physiological response of human cells to a treatment -- particularly, the response of fibroblasts to serum. A cDNA microarray was used, representing over 8,600 distinct human genes. Fibroblasts, cultured from human neonatal foreskin, were placed in a quiescent state by depriving the cells of serum for 48 hours. The fibroblasts were then stimulated by adding a medium containing 10% FBS, and the microarray was then used to measure the levels of 8,613 different mRNA sequences at 12 distinct times. The microarray was used to identify those genes (including expressed sequence tags -- ESTs) which were substantially repressed or induced and the extent of repression or induction (i.e., fold change). Five hundred seventeen genes whose mRNA levels changed in response to the treatment were selected, and graphically depicted in accordance with a hierarchy.

*Please delete the paragraph on line 26 of page 8 and replace it with the following:*

#### **1.1. CHO ~~doners~~ donors**

*Please delete the paragraph extending between pages 16 and 17 and replace it with the following paragraph:*

Initially, a database is created which relates EC (enzyme commission) numbers to coordinates on the Boehringer Mannheim biochemical pathways wall chart. This database contains current descriptions for all EC numbers and other information pertaining to the EC numbers. Descriptions of the EC numbers and other enzyme data are publicly available, and

may be obtained from the website <http://www.expasy.ch/txt/enzyme.get> the ExPASy molecular biology online server maintained by the Swiss Institute of Bioinformatics. A database may then be created linking the EC numbers with specific map coordinates corresponding to the Boehringer Mannheim biochemical pathways wall chart.

*Please delete the paragraph extending from line 5 to line 12 of page 17 and replace it with the following text:*

Once expression profiling is performed, and experiment data is obtained, EC numbers are assigned to the sequence clusters obtained in the experiment. This may involve a list of GenBank accession numbers corresponding to those affected genes affected more than two fold in a set of profiling experiments. GenBank records are publicly available at <http://www.ncbi.nlm.nih.gov/entrez/> online through the National Center for Biotechnology Information, a division of the National Library of Medicine at the United States National Institutes of Health, and may be parsed for the pattern of numbers in an EC number (###.). For every occurrence of an EC number in the GenBank file, a GenBank accession number and corresponding EC number may be written to a text file for loading into a database. The following is a sample GenBank file: illustrates the fields found in a typical Genbank file (in this case, for alcohol dehydrogenase of baboon origin. A sequence listing would typically be included in such a file, but that sequence listing is not reproduced here:

*Please delete the sequence listing extending from line 1 to line 7 of page 18.*

*Please delete the paragraph extending from line 9 to line 19 of page 18 and replace it with the following paragraph:*

If no EC number is available in the GenBank file, the nucleotide or amino acid sequence may be obtained from the GenBank file which corresponds to a particular cluster obtained from the expression profiling, and a BLAST sequence alignment may be performed, which may be performed by accessing the publicly available application through <http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=0> the online resources of the National Center for Biotechnology Information, a division of the National Library of Medicine at the United States National Institutes of Health. The GenBank file may then be

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fetches for each sequence that aligns with an expect value (E value, right-most column in the BLAST results) that is less than  $1 \times 10^{-30}$ , and by looking for EC numbers in these related sequence files. If an EC number is present, the accession number for the gene affected in the expression profiling experiment can be recorded, and the expect value from the sequence alignment may be recorded as well, along with the EC number or numbers found in the related sequence file or files.